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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,573	02/28/2002	Theodorus Petrus Maria Schetters	I 2001.004 US	3895

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AKZO NOBEL PHARMA PATENT DEPARTMENT  
PO BOX 318  
MILLSBORO, DE 19966

EXAMINER

BASKAR, PADMAVATHI

ART UNIT PAPER NUMBER

1645

DATE MAILED: 03/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/087,573	<b>Applicant(s)</b> SCHETTERS ET AL.	
	<b>Examiner</b> Padmavathi v Baskar	<b>Art Unit</b> 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 14 December 2004.  
 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.  
 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 32-35 and 64-68 is/are pending in the application.  
     4a) Of the above claim(s) 68 is/are withdrawn from consideration.  
 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
 6) ☒ Claim(s) 32-35 and 64-67 is/are rejected.  
 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.  
 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☐ All    b) ☐ Some \*    c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
         3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

*AS*  
**LYNETTE R. F. SMITH**  
**SUPERVISORY PATENT EXAMINER**  
**TECHNOLOGY CENTER 1600**

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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***Detailed Action***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's request for continued examination filed on 12/14/04 has been entered.

***Amendment***

2. Applicant's amendment filed on 12/14/04 is acknowledged and has been entered.

***Status of claims***

3. Claims 32 and 64-67 have been amended.

Claims 36-63 are canceled.

New claim 68 has been added. However, claim 68 is drawn to a non-elected invention, i.e., nucleic acid. Therefore, it is not included in the elected (protein) invention.

Claims 32-35 and 64-67 are under examination.

Claim 68 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

***Specification - Informalities***

4. It is noted that the lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors.

For example:

(1) Pages 20, 21, 28 recite sequences that are not identified by the sequence identification numbers. Further, it is noted that the sequences in the figures are not identified by

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the sequence identification numbers. Therefore, applicant is advised to insert the sequences identification numbers either in the figures or in the brief description of the drawings.

(2) The use of the trademark Diluvack<sup>®</sup> Forte on page 13 and Poly A Tract mRNA Isolation Systems<sup>®</sup> III kit on page 21 has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

(3) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, see in particular at least page 9. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

***Claim Rejections - 35 USC 112, first paragraph maintained***

5. The written description rejection of claims 32-35 and 64-68 under 35 U.S.C. 112, first paragraph is maintained as forth in the previous office action.

The claims are directed to a *Babesia canis* associated protein said protein having a molecular weight of 15 kD and comprising an amino acid sequence that is at least 80%, 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2 or immunogenic fragments of proteins that are 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2. Claims are also directed to a vaccine for combating *Babesia canis* infections comprising a protein having molecular weight of 15 kD and comprising an amino acid sequence that is at least 80% -95% homologous to the amino acid sequence as

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depicted in SEQ ID NO: 2 or immunogenic fragments of proteins that are 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2 and a pharmaceutically acceptable carrier, an adjuvant and an additional protein derived from a virus or microorganism pathogenic to dogs or a nucleic acid sequence encoding said antigen wherein said virus or micro-organism pathogenic to dogs is selected from the group of *Ehrlichia canis*, *Babesia gibsoni*, *vogeli*, *rossi*, *Leishmania donovan complex*, *Canine parvovirus*, *Canine distempervirus*, *Leptospira interrogans serovar canicola icterohaemorrhagiae*, *pomona*, *grippotyphosa*, *grippotyphosa*, *bratislava*, *Canine hepatitisvirus*, *Canine parainfluenzavirus*, *rabies virus*, *Hepatozoon canis* and *Borrelia burgdorferi*.

The specification discloses a recombinant *Babesia canis* protein having 15KD molecular weight and consisting of the amino acid sequence as set forth in SEQ.ID.NO: 2. However, the specification does not disclose *Babesia canis* protein having a molecular weight 15KD and comprising an amino acid sequence that is at least 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or immunogenic fragments of proteins that are 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2 and a vaccine for combating *B.canis* infection comprising a *Babesia canis* protein having a molecular weight of 15KD and comprising an amino acid sequence that is at least 80%, homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2. Therefore, or said variants do not meet the guidelines on written description.

(The examiner is considering all these as variants and address them as variants hereafter in the action).

The specification fails to disclose any substitution, insertion or deletion or change in (i) a protein SEQ.ID.NO: 2 to obtain variants having 80%, 85%, 90% or 95% homology to the amino acid sequence as depicted in SEQ.ID.NO: 2 or immunogenic fragments of proteins that are 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2. (ii)

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a vaccine comprising said variants or a nucleic acid encoding said variants and an additional protein derived from a virus or microorganism pathogenic to dogs, wherein said virus or microorganism pathogenic to dogs is selected from the group of *Ehrlichia canis*, *Babesia gibsoni*, *vogeli*, *rossi*, *Leishmania donovan complex*, *Canine parvovirus*, *Canine distempervirus*, *Leptospira interrogans serovar canicola icterohaemorrhagiae*, *pomona*, *grippotyphosa*, *grippotyphosa*, *bratislava*, *Canine hepatitisvirus*, *Canine parainfluenzavirus*, *rabies virus*, *Hepatozoon canis* and *Borrelia burgdorferi*.

The specification does not describe variants in vaccine preparations for combating *B.canis* infection in dogs. None of the above variants and their use in a vaccine preparation meet the written description provision of 35 U.S.C. 112, first paragraph. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Thus, the specification fails to teach variants sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed.

6. The rejection of claims 32-35 and 64-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated *Babesia canis* associated protein 15kD as determined by SDS-gel electrophoresis and consisting of SEQ.ID.NO: 2 and a vaccine composition comprising said isolated protein does not reasonably provide enablement for an isolated *Babesia canis* associated protein 15kD as determined by SDS-gel electrophoresis and is at least 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or immunogenic fragments of proteins that are 85%,

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90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2 is maintained as set forth in the previous office action.

The nature of the disclosed invention relates to cloning of nucleic acid sequences encoding a novel *Babesia canis* associated protein from *B.canis* isolate A from France that is useful for diagnostic tools for the detection of *Babesia canis* and for a vaccine composition against *B.canis* homologous strains.

The specification on pages 19-36 indicates that the claimed protein may be used as diagnostic reagent and a vaccine composition against homologous *B.canis* infections. The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for any protein that is 80% or 85% or 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or immunogenic fragments of said protein. Any substitution, insertion or deletion or change in a protein, encoded by a nucleotide sequence is highly complex and unpredictable. As taught by the prior art that even a single amino acid change in a protein leads to unpredictable changes in the biological activity of the protein. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the protein (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). Thus, it is apparent that change in a protein can lead to a loss of binding property and function of that protein. Furthermore, it is unclear whether protein that is 80% or 85% or 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or immunogenic fragments of said protein can be used as diagnostic reagent a vaccine composition. Thus, protein that is 80% or 85% or 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or immunogenic fragments of said protein. at protein level must be considered highly unpredictable, requiring a specific demonstration of efficacy on a case-by-case basis.

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The specification fails to provide an enabling disclosure for using proteins that are 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 because it fails to provide guidance how to make and use proteins that are that is 80% or 85% or 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or immunogenic fragments of said protein as a diagnostic or prophylactic reagent. The specification provides no disclosure how a protein variant of SEQ.ID.NO: 2 is used to induce a protective immune response. Absent such demonstration, the invention would require undue experimentation to practice as claimed.

Applicant's arguments filed on 12/14/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that claims have been amended to cancel "fragments" and thus overcome the rejection of record.

The examiner disagrees with the applicant because claims 32-35 are drawn to immunogenic fragments of proteins. Further, the specification does not disclose an isolated protein that are 80%, 85%, 90% or 95% homologous to the amino acid sequence as depicted in SEQ.ID.NO: 2 or immunogenic fragments of proteins that are 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2. The specification teaches an isolated polypeptide consisting of SEQ.ID.NO: 2. The examiner would like to point to the applicant that the protein as claimed is broader than SEQ.ID.NO: 2 because applicant is claiming an isolated protein comprising (open language) an amino acid sequence (less than 141 amino acid sequence) of SEQ.ID.NO: 2 plus unlimited and unknown amino acids without any structure and function. Thus, the variants (% homologous proteins) as claimed are broader than the claimed SEQ.ID.NO: 2. Please note applicant is not claiming an isolated polypeptide consisting of antigenic fragments as set forth in SEQ.ID.NO: 2.



***Claim Rejections - 35 USC § 102 maintained.***

7. The rejection of claims 32-35 and 64 –66 and 67 under 35 U.S.C. 102(b) as being anticipated by Schetters et al 1992 (PARASITE IMMUNOLOGY 1992, 14(3) 295-305 abstract only) is maintained as set forth in the previous office action.

Schetters et al disclose a vaccine comprising *Babesia* associated protein obtained from *Babesia canis* cultures and adjuvant (see abstract). In the absence of evidence to the contrary the disclosed prior art protein obtained from cultures comprises *B. canis* associated protein 15KD antigen comprising SEQ ID NO: 2 or immunogenic fragments of proteins that are 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2. Characteristic such as SEQ.ID.NO: 2 is considered as an inherent property of the disclosed vaccine comprising *B. canis* protein. Examiner is viewing the claims as having open claim language (i.e., comprising) Applicant's use of the open-ended term "comprising " in claims fails to include unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts). See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948) and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the disclosed prior art composition and the claimed composition are the same. Since the Office does not have the facilities for examining and comparing applicants' claimed composition with the composition of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed composition and the composition of the prior art. It is acknowledged that weight is given to every term in claims. This is why the instant claims drawn to pharmaceutical compositions and vaccine are scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine compositions must be weighed with the structural limitations of the claim. If the vaccine compositions merely comprise a known composition comprising protein, the term carries little

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weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Here, the prior art teaches the same composition comprising said protein as claimed. In re Thorpe, 227 U.S.P.Q. 964, 966 (Fed. Cir. 1985). In re Marosi, 218 U.S.P.Q. 289, 293-293 (C.A.F.C. 1983). In re Best, 195 U.S.P.Q. 430, 433 (C.C.P.A. 1977). In re Brown, 173 U.S.P.Q. 685, 688 (C.C.P.A. 1972). Thus the prior art anticipated the claimed invention.

Applicant's arguments filed on 12/14/05 have been fully considered but they are not deemed to be persuasive.

Applicant states that the prior art proteins in the supernatant are exo-antigens and the claimed Bcvir15 and Hcvir15 are not exoantigens. The proteins in the supernatant are exo-antigen and are the subject of US patent 6,045,806. Applicant further describes the differences between the two proteins and states that the exo-antigens of the prior art are not recognized by an antiserum specific for 15kD antigen and brings examiner's attention to figure 8 and specification pages 29-30.

The examiner reviewed the suggested figures and specification and understands the applicant's invention. However, the examiner has rejected the claims based on the language and limitations (open language such as having, comprising and %homologous proteins etc) used in the claims. As the claim recites an isolated protein "having" or "an immunogenic fragment of said protein" read on the prior art because applicant is claiming any isolated protein having an amino acid sequence that is homologous to SEQ.ID.NO: 2 or immunogenic fragments of proteins that are 85%, 90% and 95% homologous to the amino acid sequence as depicted in SEQ ID NO: 2. Therefore, any two amino acids of the prior art read on the claimed invention. Further, the limitations such as "Bcvir 15, antiserum specific for Bcvir 15, precipitated from total

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antigen fraction" which applicant is arguing are characteristics of the protein and are not set forth in the claims. Therefore, the rejection is maintained.

**Remarks**

8. No claims are allowed.

**Conclusion**

9. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The RightFax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

  
Padma Baskar Ph.D.

3/5/05